Complete Summary

GUIDELINE TITLE

Global strategy for asthma management and prevention.

BIBLIOGRAPHIC SOURCE(S)

Global Initiative for Asthma (GINA), National Heart, Lung and Blood Institute (NHLBI). Global strategy for asthma management and prevention. Bethesda (MD): Global Initiative for Asthma (GINA), National Heart, Lung and Blood Institute (NHLBI); 2008. 92 p. [383 references]

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Global Initiative for Asthma (GINA), National Heart, Lung and Blood Institute (NHLBI). Global strategy for asthma management and prevention. Bethesda (MD): Global Initiative for Asthma (GINA), National Heart, Lung and Blood Institute (NHLBI); 2007. 92 p. [372 references]

In an effort to keep the GINA Workshop report as up to date as possible, a GINA Science Committee has been established to review published research on asthma management and prevention, and to post yearly updates on the GINA Web site. See the GINA Web site for archived versions of the GINA guidelines.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Asthma

GUIDELINE CATEGORY

Counseling
Diagnosis
Evaluation
Management
Prevention
Treatment

CLINICAL SPECIALTY

Allergy and Immunology
Emergency Medicine
Family Practice
Internal Medicine
Nursing
Pediatrics
Preventive Medicine
Pulmonary Medicine

INTENDED USERS

Advanced Practice Nurses
Emergency Medical Technicians/Paramedics
Health Care Providers
Health Plans
Managed Care Organizations
Nurses
Physician Assistants
Physicians
Public Health Departments
Respiratory Care Practitioners

GUIDELINE OBJECTIVE(S)

- To present information about asthma management in as comprehensive manner as possible but not in the detail that would normally be found in a textbook
- To develop a network of individuals, organizations, and public health officials to disseminate information about the care of patients with asthma while at the same time assuring a mechanism to incorporate the results of scientific investigations into asthma care
- To present a comprehensive plan to manage asthma with the goal of reducing chronic disability and premature deaths while allowing patients with asthma to lead productive and fulfilling lives
- To provide public health officials with information about the costs of asthma care, how to effectively manage this chronic disorder, and education methods to develop asthma care services and programs responsive to the particular needs and circumstances within their countries

TARGET POPULATION

Patients of all ages in countries throughout the world with asthma

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis and Classification

1. Clinical diagnosis
    - Medical history and physical examination
    - Consideration of signs and symptoms
    - Measurements of lung function via spirometry or peak expiratory flow
    - Measurements of allergic status
    - Consideration of challenges diagnosing asthma in children 5 years and younger and in the elderly, and occupational asthma
    - Measurement of airway responsiveness
2. Consideration of severity
3. Classification of asthma based on level of control (clinical control, frequency of symptoms, limitations, need for reliever treatment)

Management, Prevention and Treatment

1. Development of patient-doctor relationship
    - Patient education, including self-monitoring
    - Personal asthma treatment action plan
2. Identification and reduction of risk factors, including exacerbation triggers and occupational sensitizers
3. Assessment, treatment and monitoring of asthma
    - Assessment of control based on daytime and nocturnal symptoms, activity limitations, need for reliever/rescue treatment, lung function, and exacerbations
    - Assessment of patient adherence to treatment
    - Treatment to achieve control
        - Use of stepped system that includes as-needed reliever medications alone and reliever plus one or more controllers
    - Treatment to maintain control
        - Stepping down treatment when asthma is controlled
        - Stepping up treatment in response to loss of control

4. Management of asthma exacerbations
    - Assessment of severity
    - Management in community settings
        - Bronchodilators
        - Glucocorticosteroids
    - Management in acute care settings
        - Assessment
        - Treatment with oxygen, rapid-acting inhaled $beta_2$ agonists, epinephrine, and additional bronchodilators
        - Consideration of discharge versus hospitalization

5. Consideration of special circumstances, including pregnancy; surgery; rhinitis, sinusitis, and nasal polyps; occupational asthma; respiratory infections; gastroesophageal reflux; aspirin-induced asthma; and anaphylaxis

MAJOR OUTCOMES CONSIDERED

- Frequency and severity of asthma symptoms, including nocturnal
- Frequency of exacerbation of symptoms
- Limitations of daily activities, including physical exercise
- Requirement for rescue medications
- Changes in lung function peak expiratory flow or fraction of expired volume in 1 second
- Frequency of emergency department visits and hospitalization
- Morbidity, including quality of life, due to exacerbations and chronic symptoms
- Mortality
- Socioeconomic burden

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The process to produce this 2008 update included a Pub Med search using search fields established by the Committee: 1) *asthma, All Fields, All ages, only items with abstracts, Clinical Trial, Human, sorted by Authors*; and 2) *asthma AND systematic, All fields, ALL ages, only items with abstracts, Human, sorted by author*. In addition, publications in peer review journals not captured by Pub Med could be submitted to individual members of the Committee providing an abstract and the full paper were submitted in (or translated into) English.

Between July 1, 2007 and June 30, 2008, 406 articles met the search criteria; 10 additional publications were brought to the attention of the committee. Of the 416 articles, 40 papers were identified to have an impact on the Global Initiative for Asthma (GINA) Report (updated 2007) that was posted on the website in December 2007 either by: 1) confirming, that is, adding or replacing an existing reference, or 2) modifying, that is, changing the text or introducing a concept requiring a new recommendation to the report. The summary is reported in three segments: A) Modifications in the text; B) References that provided confirmation or an update of previous recommendations; and C) Changes or modifications to the text.

The major goal of the revision was to present information about asthma management in as comprehensive manner as possible but not in the detail that would normally be found in a textbook. Every effort was made to select key references, although in many cases, several other publications could have been cited.

Diagnosis and Management of Asthma in Children 5 Years and Younger:
Throughout 2008, several pediatric experts have been developing a report that

will focus on asthma care in children 5 years and younger. The document is expected to be released in early 2009. Publications that appeared during the 2008 update cycle that impact on this young age group will be reviewed in preparation of the new report (see section C.2. in the original guideline document) and are not included in this 2008 update.

NUMBER OF SOURCE DOCUMENTS

Between July 1, 2007 and June 30, 2008, 40 papers were identified to have an impact on the Global Initiative for Asthma (GINA) Report (updated 2007)

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus (Committee)
Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Evidence Category	Sources of Evidence	Definition
A	Randomized controlled trials (RCTs). Rich body of data	Evidence is from endpoints of well-designed RCTs that provide a consistent pattern of findings in the population for which the recommendation is made. Category A requires substantial numbers of studies involving substantial numbers of participants.
B	Randomized controlled trials. Limited body of data.	Evidence is from endpoints of intervention studies that include only a limited number of patients, post hoc or subgroup analysis of RCTs, or meta-analysis of RCTs. In general, Category B pertains when few randomized trials exist, they are small in size, they were undertaken in a population that differs from the target population of the recommendation, or the results are somewhat inconsistent.

Evidence Category	Sources of Evidence	Definition
C	Nonrandomized trials. Observational studies.	Evidence is from outcomes of uncontrolled or nonrandomized trials or from observational studies.
D	Panel consensus judgment.	This category is used only in cases where the provision of some guidance was deemed valuable but the clinical literature addressing the subject was deemed insufficient to justify placement in one of the other categories. The Panel Consensus is based on clinical experience or knowledge that does not meet the above-listed criteria.

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

All members of the Committee received a summary of citations and all abstracts. Each abstract was assigned to two Committee members, although all members were offered the opportunity to provide an opinion on any abstract. Members evaluated the abstract or, up to her/his judgment, the full publication, by answering specific written questions from a short questionnaire, and to indicate if the scientific data presented impacted on recommendations in the Global Initiative for Asthma (GINA) report. If so, the member was asked to specifically identify modifications that should be made. The entire GINA Science Committee met on a regular basis to discuss each individual publication that was indicated to have an impact on asthma management and prevention by at least 1 member of the Committee, and to reach a consensus on the changes in the report. Disagreements were decided by vote.

In preparation of GINA reports, including this 2008 update, grading of evidence has been completed using four categories (see the "Rating Scheme for the Strength of the Evidence" field). However, a new methodology called the GRADE system has been described and is being widely adopted. GINA is concerned with regard to the resource implications of this change, especially given the already rigorous method of reviewing the literature and updating recommendations that is already in place. Nonetheless, a system is being developed to slowly make a

transition to the GRADE methodology by initially identifying key recommendations that require more in-depth evaluation, and to implement the creation and evaluation of evidence tables. Attention will be paid to ensuring clarity of the recommendations based on these tables. The 2009 update will begin to reflect this work. (See section C.3 in the original guideline document.)

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

2006 Guideline

In January 2005, the Global Initiative for Asthma (GINA) Science Committee initiated its work on this new report. During a two-day meeting, the Committee established that the main theme of the new report should be the control of asthma. A table of contents was developed, themes for each chapter identified, and writing teams formed. The Committee met in May and September 2005 to evaluate progress and to reach consensus on messages to be provided in each chapter. Throughout its work, the Committee made a commitment to develop a document that would reach a global audience, be based on the most current scientific literature, and be as concise as possible, while at the same time recognizing that one of the values of the GINA Report has been to provide background information about asthma management and the scientific information on which management recommendations are based.

In January 2006, the Committee met again for a two-day session during which another in-depth evaluation of each chapter was conducted. At this meeting, members reviewed the literature that appeared in 2005—using the same criteria developed for the update process. The list of 285 publications from 2005 that were considered is posted on the GINA website. At the January meeting, it was clear that work remaining would permit the report to be finished during the summer of 2006 and, accordingly, the Committee requested that as publications appeared throughout early 2006, they be reviewed carefully for their impact on the recommendations. At the Committee's next meeting in May, 2006 publications meeting the search criteria were considered and incorporated into the current drafts of the chapters, where appropriate. A final meeting of the Committee was held be held in September 2006, at which publications that appear prior to July 31, 2006 were considered for their impact on the document.

2008 Update

The first update of the 2006 report (2007 update) included the impact of publications from July 1, 2006 through June 30, 2007. This second update of the 2006 report (2008 update) includes the impact of publications from July 1, 2007 through June 30, 2008.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

Cost is recognized as an important barrier to the delivery of optimal evidence-based health care in almost every country, although its impact on patients' access to treatments varies widely both between and within countries. At the country or local level, health authorities make resource availability and allocation decisions affecting populations of asthma patients by considering the balance and tradeoffs between costs and clinical outcomes (benefits and harms), often in relation to competing public health and medical needs. Treatment costs must also be explicitly considered at each consultation between health care provider and patient to assure that cost does not present a barrier to achieving asthma control. Thus, those involved in the adaptation and implementation of asthma guidelines require an understanding of the cost and cost effectiveness of various management recommendations in asthma care. To this end, a short discussion of cost-effectiveness evaluation for asthma care, including utilization and cost of health care resources and determining the economic value of interventions in asthma, can be found in the original guideline document.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

2006 Guideline

Members of the Global Initiative for Asthma (GINA) Assembly were invited to submit comments on a DRAFT document during the summer of 2006. Their comments, along with comments received from several individuals who were invited to serve as reviewers, were considered by the Committee in September 2006.

2007 and 2008 Updates

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Evidence grades (A-D) are defined and provided at the end of the "Major Recommendations" field.

2008 Summary of Major Changes

Some of the major changes that have been made in this report include:

1. Every effort has been made to produce a more streamlined document that will be of greater use to busy clinicians, particularly primary care professionals. The document is referenced with the up-to-date sources so that interested readers may find further details on various topics that are summarized in the report.
2. The whole of the document now emphasizes asthma control. There is now good evidence that the clinical manifestations of asthma—symptoms, sleep disturbances, limitations of daily activity, impairment of lung function, and use of rescue medications—can be controlled with appropriate treatment.
3. Updated epidemiological data, particularly drawn from the report *Global Burden of Asthma*, are summarized. Although from the perspective of both the patient and society the cost to control asthma seems high, the cost of not treating asthma correctly is even higher.
4. The concept of difficult-to-treat asthma is introduced and developed at various points throughout the report. Patients with difficult-to-treat asthma are often relatively insensitive to the effects of glucocorticosteroid medications, and may sometimes be unable to achieve the same level of control as other asthma patients.
5. Lung function testing by spirometry or peak expiratory flow (PEF) continues to be recommended as an aid to diagnosis and monitoring. Measuring the *variability* of airflow limitation is given increased prominence, as it is key to both asthma diagnosis and the assessment of asthma control.
6. The previous classification of asthma by severity into Intermittent, Mild Persistent, Moderate Persistent, and Severe\Persistent is now recommended only for research purposes.
7. Instead, the document now recommends a classification of asthma by level of control: Controlled, Partly Controlled, or Uncontrolled. This reflects an understanding that asthma severity involves not only the severity of the underlying disease but also its responsiveness to treatment, and that severity is not an unvarying feature of an individual patient's asthma but may change over months or years.
8. Throughout the report, emphasis is placed on the concept that the goal of asthma treatment is to achieve and maintain clinical control. Asthma control is defined as:
    - No (twice or less/week) daytime symptoms
    - No limitations of daily activities, including exercise
    - No nocturnal symptoms or awakening because of asthma
    - No (twice or less/week) need for reliever treatment
    - Normal or near-normal lung function results
    - No exacerbations
9. Emphasis is given to the concept that increased use, especially daily use, of reliever medication is a warning of deterioration of asthma control and indicates the need to reassess treatment.
10. The roles in therapy of several medications have evolved since previous versions of the report:
    - Recent data indicating a possible increased risk of asthma-related death associated with the use of long-acting $beta_2$-agonists in a small group of individuals has resulted in increased emphasis on the message that long-acting $beta_2$-agonists should not be used as monotherapy in asthma, and must only be used in combination with an appropriate dose of inhaled glucocorticosteroid.
    - Leukotriene modifiers now have a more prominent role as controller treatment in asthma, particularly in adults. Long-acting oral $beta_2$-

agonists alone are no longer presented as an option for add-on treatment at any step of therapy, unless accompanied by inhaled glucocorticosteroids.
- Monotherapy with cromones is no longer given as an alternative to monotherapy with a low dose of inhaled glucocorticosteroids in adults.
- Some changes have been made to the tables of equipotent daily doses of inhaled glucocorticosteroids for both children and adults.

11. The six-part asthma management program detailed in previous versions of the report has been changed. The current program includes the following five components:

    Component 1. Develop Patient/Doctor Partnership

    Component 2. Identify and Reduce Exposure to Risk Factors

    Component 3. Assess, Treat, and Monitor Asthma

    Component 4. Manage Asthma Exacerbations

    Component 5. Special Considerations

12. The inclusion of Component 1 reflects the fact that effective management of asthma requires the development of a partnership between the person with asthma and his or her health care professional(s) (and parents/caregivers, in the case of children with asthma). The partnership is formed and strengthened as patients and their health care professionals discuss and agree on the goals of treatment, develop a personalized, written self-management action plan including self-monitoring, and periodically review the patient's treatment and level of asthma control. Education remains a key element of all doctor-patient interactions.
13. Component 3 presents an overall concept for asthma management oriented around the new focus on asthma control. Treatment is initiated and adjusted in a continuous cycle (assessing asthma control, treating to achieve control, and monitoring to maintain control) driven by the patients level of asthma control.
14. Treatment options are organized into five "Steps" reflecting increasing intensity of treatment (dosages and/or number of medications) required to achieve control. At all Steps, a reliever medication should be provided for as needed use. At Steps 2 through 5, a variety of controller medications are available.
15. If asthma is not controlled on the current treatment regimen, treatment should be stepped up until control is achieved. When control is maintained, treatment can be stepped down in order to find the lowest step and dose of treatment that maintains control.
16. Although each component contains management advice for all age categories where these are considered relevant, special challenges must be taken into account in making recommendations for managing asthma in children in the first 5 years of life. Accordingly, an Executive Summary has been prepared—and appears at the end of this introduction—that extracts sections on diagnosis and management for this very young age group.
17. It has been demonstrated in a variety of settings that patient care consistent with evidence-based asthma guidelines leads to improved outcomes.

However, in order to effect changes in medical practice and consequent improvements in patient outcomes, evidence-based guidelines must be implemented and disseminated at national and local levels. Thus, a chapter has been added on implementation of asthma guidelines in health systems that details the process and economics of guideline implementation.

Definition and Overview

Key Points

- Asthma is a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role. The chronic inflammation is associated with airway hyperresponsiveness that leads to recurrent episodes of wheezing, breathlessness, chest tightness, and coughing, particularly at night or in the early morning. These episodes are usually associated with widespread, but variable, airflow obstruction within the lung that is often reversible either spontaneously or with treatment.
- Clinical manifestations of asthma can be controlled with appropriate treatment. When asthma is controlled, there should be no more than occasional flare-ups and severe exacerbations should be rare.
- Asthma is a problem worldwide, with an estimated 300 million affected individuals.
- Although from the perspective of both the patient and society the cost to control asthma seems high, the cost of not treating asthma correctly is even higher.
- A number of factors that influence a person's risk of developing asthma have been identified. These can be divided into host factors (primarily genetic) and environmental factors.
- The clinical spectrum of asthma is highly variable, and different cellular patterns have been observed, but the presence of airway inflammation remains a consistent feature.

Factors Influencing the Development and Expression of Asthma

HOST FACTORS

Genetic, e.g.,

- Genes pre-disposing to atopy
- Genes pre-disposing to airway hyperresponsiveness

Obesity

Sex

ENVIRONMENTAL FACTORS

Factors Influencing the Development and Expression of Asthma
Allergens • Indoor: Domestic mites, furred animals (dogs, cats, mice), cockroach allergen, fungi, molds, yeasts • Outdoor: Pollens, fungi, molds, yeasts Infections (predominantly viral) Occupational sensitizers* Tobacco smoke • Passive smoking • Active smoking Outdoor/Indoor Air Pollution Diet

*See Figure 1-3 in the original guideline document for examples of agents causing asthma in selected occupations.

Diagnosis and Classification

Key Points

- A clinical diagnosis of asthma is often prompted by symptoms such as episodic breathlessness, wheezing, cough, and chest tightness.
- Measurements of lung function (spirometry or PEF) provide an assessment of the severity of airflow limitation, its reversibility, and its variability, and provide confirmation of the diagnosis of asthma.
- Measurements of allergic status can help to identify risk factors that cause asthma symptoms in individual patients.
- Extra measures may be required to diagnose asthma in children 5 years and younger and in the elderly, and occupational asthma.
- For patients with symptoms consistent with asthma, but normal lung function, measurement of airway responsiveness may help establish the diagnosis.
- Asthma has been classified by severity in previous reports (see Figure 2-4 in the original guideline document). However, asthma severity may change over time, and depends not only on the severity of the underlying disease but also its responsiveness to treatment.
- To aid in clinical management, a classification of asthma by level of control is recommended (see Figure 2-5 in the original guideline document).
- Clinical control of asthma is defined as:
    - No (twice or less/week) daytime symptoms
    - No limitations of daily activities, including exercise
    - No nocturnal symptoms or awakening because of asthma
    - No (twice or less/week) need for reliever treatment
    - Normal or near-normal lung function

- No exacerbations

Refer to the original guideline document for more details about the diagnosis and classification of asthma.

Asthma Treatments

Key Points

- Medications to treat asthma can be classified as controllers or relievers. Controllers are medications taken daily on a long-term basis to keep asthma under clinical control chiefly through their anti-inflammatory effects. Relievers are medications used on an as-needed basis that act quickly to reverse bronchoconstriction and relieve its symptoms.
- Asthma treatment can be administered in different ways—inhaled, orally, or by injection. The major advantage of inhaled therapy is that drugs are delivered directly into the airways, producing higher local concentrations with significantly less risk of systemic side effects.
- Inhaled glucocorticosteroids are the most effective controller medications currently available.
- Rapid-acting inhaled $beta_2$-agonists are the medications of choice for relief of bronchoconstriction and for the pretreatment of exercise-induced bronchoconstriction, in both adults and children of all ages.
- Increased use, especially daily use, of reliever medication is a warning of deterioration of asthma control and indicates the need to reassess treatment.

Refer to the original guideline document for more information about specific controller and reliever medications, including information about asthma treatment in children.

Asthma Management and Prevention

Introduction

Asthma has a significant impact on individuals, their families, and society. Although there is no cure for asthma, appropriate management that includes a partnership between the physician and the patient/family most often results in the achievement of control.

The goals for successful management of asthma are to:

- Achieve and maintain control of symptoms
- Maintain normal activity levels, including exercise
- Maintain pulmonary function as close to normal as possible
- Prevent asthma exacerbations
- Avoid adverse effects from asthma medications
- Prevent asthma mortality

These goals for therapy reflect an understanding of asthma as a chronic inflammatory disorder of the airways characterized by recurrent episodes of wheezing, breathlessness, chest tightness, and coughing. Clinical studies have shown that asthma can be effectively controlled by intervening to suppress and reverse the inflammation as well as treating the bronchoconstriction and related symptoms. Furthermore, early intervention to stop exposure to the risk factors that sensitized the airway may help improve the control of asthma and reduce medication needs. Experience in occupational asthma indicates that long-standing exposure to sensitizing agents may lead to irreversible airflow limitation.

The management of asthma can be approached in different ways, depending on the availability of the various forms of asthma treatment and taking into account cultural preferences and differing health care systems. The recommendations in this section reflect the current scientific understanding of asthma. They are based as far as possible on controlled clinical studies, and the text references many of these studies. For those aspects of the clinical management of asthma that have not been the subject of specific clinical studies, recommendations are based on literature review, clinical experience, and expert opinion of project members.

The recommendations for asthma management are laid out in five interrelated components of therapy:

1. Develop Patient/Doctor Partnership
2. Identify and Reduce Exposure to Risk Factors
3. Assess, Treat, and Monitor Asthma
4. Manage Asthma Exacerbations
5. Special Considerations

Component 1: Develop Patient/Doctor Relationship

Key Points

- The effective management of asthma requires the development of a partnership between the person with asthma and his or her health care professional(s) (and parents/caregivers, in the case of children with asthma).
- The aim of this partnership is guided self-management—that is, to give people with asthma the ability to control their own condition with guidance from health care professionals.
- The partnership is formed and strengthened as patients and their health care professionals discuss and agree on the goals of treatment, develop a personalized, written self-management plan including self-monitoring, and periodically review the patient's treatment and level of asthma control.
- Education should be an integral part of all interactions between health care professionals and patients, and is relevant to asthma patients of all ages.
- Personal asthma action plans help individuals with asthma make changes to their treatment in response to changes in their level of asthma control, as indicated by symptoms and/or peak expiratory flow, in accordance with written predetermined guidelines.

See "Essential Features of the Doctor-Patient Partnership to Achieve Guided Self-Management in Asthma" below. This approach is called guided self-management and has been shown to reduce asthma morbidity in both adults (**Evidence A**) and children (**Evidence A**).

Essential Features of the Doctor-Patient Partnership to Achieve Guided Self-Management in Asthma
• Education • Joint setting of goals • Self-monitoring. The person with asthma is taught to combine assessment of asthma control with educated interpretation of key symptoms. • Regular review of asthma control, treatment, and skills by a health care professional • Written action plan. The person with asthma is taught which medications to use regularly and which to use as needed, and how to adjust treatment in response to worsening asthma control. • Self-monitoring is integrated with written guidelines for both the long-term treatment of asthma and the treatment of asthma exacerbations.

Asthma Education

Education should be an integral part of all interactions between health care professionals and patients, and is relevant to asthma patients of all ages. Although the focus of education for small children will be on the parents and caregivers, children as young as 3 years of age can be taught simple asthma management skills. Adolescents may have some unique difficulties regarding adherence that may be helped through peer support group education in addition to education provided by the health care professional.

The table below outlines the key features and components of an asthma education program. The information and skills training required by each person may vary, and their ability or willingness to take responsibility similarly differs. Thus all individuals require certain core information and skills, but most education must be personalized and given to the person in a number of steps. Social and psychological support may also be required to maintain positive behavioral change.

Education and the Patient/Doctor Partnership
Goal: To provide the person with asthma, their family, and other caregivers with suitable information and training so that they can keep well and adjust treatment according to a medication plan developed with the health care professional **Key components**: • Focus on the development of the partnership • Acceptance that this is a continuing process • A sharing of information • Full discussion of expectations

Education and the Patient/Doctor Partnership
• Expression of fears and concerns **Provide specific information, training, and advice about**: • Diagnosis • Difference between "relievers" and "controllers" • Potential side effects of medications • Use of inhaler devices • Prevention of symptoms and attacks • Signs that suggest asthma is worsening and actions to take • Monitoring control of asthma • How and when to seek medical attention **The person then requires**: • A guided self-management plan • Regular supervision, revision, reward, and reinforcement

Good communication is essential as the basis for subsequent good compliance/adherence (**Evidence B**).

Key factors that facilitate good communication are:

- A congenial demeanor (friendliness, humor, and attentiveness)
- Engaging in interactive dialogue
- Giving encouragement and praise
- Empathy, reassurance, and prompt handling of any concerns
- Giving of appropriate (personalized) information
- Eliciting shared goals
- Feedback and review

See the original guideline document for more information about developing the patient/doctor relationship.

Personal Asthma Action Plans

Personal asthma action plans help individuals with asthma make changes to their treatment in response to changes in their level of asthma control, as indicated by symptoms and/or peak expiratory flow, in accordance with written predetermined guidelines.

The effects were greatest where the intervention involved each of the following elements: education, self-monitoring, regular review, and patient-directed self-management using a written self-management action plan (**Evidence A**). Patients experience a one-third to two-thirds reduction in hospitalizations, emergency room visits, unscheduled visits to the doctor for asthma, missed days of work, and nocturnal wakening. It has been estimated that the implementation of a self-management program in 20 patients prevents one hospitalization, and successful

completion of such a program by eight patients prevents one emergency department visit. Less intensive interventions that involve self-management education but not a written plan are less effective. The efficacy is similar regardless of whether patients self-adjust their medications according to an individual written plan or adjustments of medication are made by a doctor. (**Evidence B**).

Education of Others

Specific advice about asthma and its management should be offered to school teachers and physical education instructors, and several organizations produce materials for this purpose. Schools may need advice on improving the environment and air quality for children with asthma. It is also helpful for employers to have access to clear advice about asthma. Most occupations are as suitable for those with asthma as for those without, but there may be some circumstances where caution is needed. See the original guideline document for more information.

Component 2: Identify and Reduce Exposure to Risk Factors

Key Points

- Pharmacologic intervention to treat established asthma is highly effective in controlling symptoms and improving quality of life. However, measures to prevent the development of asthma, asthma symptoms, and asthma exacerbations by avoiding or reducing exposure to risk factors should be implemented wherever possible.
- At this time, few measures can be recommended for prevention of asthma because the development of the disease is complex and incompletely understood.
- Asthma exacerbations may be caused by a variety of risk factors, sometimes referred to as "triggers," including allergens, viral infections, pollutants, and drugs.
- Reducing a patient's exposure to some categories of risk factors improves the control of asthma and reduces medication needs.
- The early identification of occupational sensitizers and the removal of sensitized patients from any further exposure are important aspects of the management of occupational asthma.

Introduction

Although pharmacologic intervention to treat established asthma is highly effective in controlling symptoms and improving quality of life, measures to prevent the development of asthma, asthma symptoms, and asthma by avoiding or reducing exposure to risk factors should be implemented wherever possible. At this time, few measures can be recommended for prevention of asthma because the development of the disease is complex and incompletely understood. This area is a focus of intensive research, but until such measures are developed prevention efforts must primarily focus on prevention of asthma symptoms and attacks.

Asthma Prevention

Measures to prevent asthma may be aimed at the prevention of allergic sensitization (i.e., the development of atopy, likely to be most relevant prenatally and perinatally), or the prevention of asthma development in sensitized people. Other than preventing tobacco exposure both *in utero* and after birth, there are no proven and widely accepted interventions that can prevent the development of asthma.

Exposure to tobacco smoke both prenatally and postnatally is associated with measurable harmful effects, including effects on lung development and a greater risk of developing wheezing illnesses in childhood. Although there is little evidence that maternal smoking during pregnancy has an effect on allergic sensitization, passive smoking increases the risk of allergic sensitization in children. Both prenatal and postnatal maternal smoking is problematic. Pregnant women and parents of young children should be advised not to smoke (**Evidence B**).

See the original guideline document for a discussion of other topics related to asthma prevention.

Prevention of Asthma Symptoms and Exacerbations

Asthma exacerbations may be caused by a variety of factors, sometimes referred to as "triggers," including allergens, viral infections, pollutants, and drugs. Reducing a patient's exposure to some of these categories of risk factors (e.g., smoking cessation, reducing exposure to secondhand smoke, reducing or eliminating exposure to occupational agents known to cause symptoms, and avoiding foods/additives/drugs known to cause symptoms) improves the control of asthma and reduces medication needs. In the case of other factors (e.g., allergens, viral infections and pollutants), measures where possible should be taken to avoid these. Because many asthma patients react to multiple factors that are ubiquitous in the environment, avoiding these factors completely is usually impractical and very limiting to the patient. Thus, medications to maintain asthma control have an important role because patients are often less sensitive to these risk factors when their asthma is under good control.

Indoor Allergens

Domestic Mites

No single measure is likely to reduce exposure to mite allergens, and single chemical and physical methods aimed at reducing mite allergens are not effective in reducing asthma symptoms in adults (**Evidence A**). One study showed some efficacy of mattress encasing at reducing airway hyperresponsiveness in children (**Evidence B**). An integrated approach including barrier methods, dust removal and reduction of microhabitats favorable to mites has been suggested, although its efficacy at reducing symptoms has only been confirmed in deprived populations with a specific environmental exposure (**Evidence B**) and a recommendation for its widespread use cannot be made.

Cockroaches

Avoidance measures for cockroaches include eliminating suitable environments (restricting havens by caulking and sealing cracks in the plasterwork and flooring, controlling dampness, and reducing the availability of food), restricting access (sealing entry sources such as around paperwork and doors), chemical control, and traps. However, these measures are only partially effective in removing residual allergens (**Evidence C**).

Indoor Air Pollutants

The most important measure in controlling indoor air pollutants is to avoid passive and active smoking. Secondhand smoke increases the frequency and severity of symptoms in children with asthma. Parents/caregivers of children with asthma should be advised not to smoke and not to allow smoking in rooms their children use. In addition to increasing asthma symptoms and causing long-term impairments in lung function, active cigarette smoking reduces the efficacy of inhaled and systemic glucocorticosteroids (**Evidence B**), and smoking cessation needs to be vigorously encouraged for all patients with asthma who smoke. Other major indoor air pollutants include nitric oxide, nitrogen oxides, carbon monoxide, carbon dioxide, sulfur dioxide, formaldehyde, and biologicals (endotoxin). However, methods to control or prevent exposure to these pollutants, such as venting all furnaces to the outdoors, and maintaining heating systems adequately, have not been adequately evaluated and can be expensive (**Evidence D**).

Outdoor Air Pollutants

Avoidance of unfavorable environmental conditions is usually unnecessary for patients whose asthma is controlled. For patients with asthma that is difficult to control, practical steps to take during unfavorable environmental conditions include avoiding strenuous physical activity in cold weather, low humidity, or high air pollution; avoiding smoking and smoke-filled rooms; and staying indoors in a climate-controlled environment.

Occupational Exposures

The early identification of occupational sensitizers and the removal of sensitized patients from any further exposure are important aspects of the management of occupational asthma (**Evidence B**). Once a patient has become sensitized to an occupational allergen, the level of exposure necessary to induce symptoms may be extremely low, and resulting exacerbations become increasingly severe. Attempts to reduce occupational exposure have been successful especially in industrial settings, and some potent sensitizers, such as soy castor bean, have been replaced by less allergenic substances (**Evidence B**). Prevention of latex sensitization has been made possible by the production of hypoallergenic gloves, which are powder free and have a lower allergen content (**Evidence C**).

Food and Food Additives

When food allergy is demonstrated, food allergen avoidance can reduce asthma exacerbations (**Evidence D**).

Drugs

Some medications can exacerbate asthma. Aspirin and other nonsteroidal anti-inflammatory drugs can cause severe exacerbations and should be avoided in patients with a history of reacting to these agents. Beta-blocker drugs administered orally or intraocularly may exacerbate bronchospasm (**Evidence A**) and close medical supervision is essential when these are used by patients with asthma.

Obesity

Increases in body mass index (BMI) have been associated with increased prevalence of asthma, although the mechanisms behind this association are unclear. Weight reduction in obese patients with asthma has been demonstrated to improve lung function, symptoms, morbidity, and health status (**Evidence B**).

See the original guideline document for a more detailed discussion of risk factors, including indoor and outdoor allergens, indoor and outdoor air pollutants, occupational exposures, food and food additives, drugs, influenza vaccination, obesity, emotional stress, and other factors that may exacerbate asthma.

Component 3: Assess, Treat, and Monitor Asthma

Key Points

- The goal of asthma treatment, to achieve and maintain clinical control, can be reached in a majority of patients with a pharmacologic intervention strategy developed in partnership between the patient/family and the doctor.
- Treatment should be adjusted in a continuous cycle driven by the patients' asthma control status. If asthma is not controlled on the current treatment regimen, treatment should be stepped up until control is achieved. When control is maintained for at least three months, treatment can be stepped down.
- In treatment-naïve patients with persistent asthma, treatment should be started at *Step 2*, or, if very symptomatic (uncontrolled), at *Step 3*. For *Steps 2* through *5*, a variety of controller medications are available.
- At each treatment step, reliever medication should be provided for quick relief of symptoms as needed.
- Ongoing monitoring is essential to maintain control and to establish the lowest step and dose of treatment to minimize cost and maximize safety.

Introduction

The goal of asthma treatment, to achieve and maintain clinical control, can be reached in the majority of patients with a pharmacologic intervention strategy developed in partnership between the patient/family and the doctor. Each patient is assigned to one of five "treatment steps" depending on their current level of control and treatment is adjusted in a continuous cycle driven by changes in their asthma control status. This cycle involves:

- Assessing Asthma Control
- Treating to Achieve Control

- Monitoring to Maintain Control

In this Component, this cycle is described for long-term treatment of asthma. Treatment for exacerbations is detailed in Component 4, below.

Assessing Asthma Control

Each patient should be assessed to establish his or her current treatment regimen, adherence to the current regimen, and level of asthma control. A simplified scheme for recognizing controlled, partly controlled, and uncontrolled asthma in a given week is provided in the table below. This is a working scheme based on current opinion and has not been validated. Several composite control measures (e.g., Asthma Control Test, Asthma Control Questionnaire, Asthma Therapy Assessment Questionnaire, Asthma Control Scoring System) have been developed and are being validated for various applications, including use by health care providers to assess the state of control of their patients' asthma and by patients for self-assessments as part of a written personal asthma action plan. Uncontrolled asthma may progress to the point of an exacerbation, and immediate steps, described in Component 4, should be taken to regain control.

Levels of Asthma Control			
Characteristic	**Controlled (All of the following)**	**Partly Controlled (Any measure present in any week)**	**Uncontrolled**
Daytime symptoms	None (twice or less/week)	More than twice/week	**Three or more features of partly controlled asthma present in any week**
Limitations of activities	None	Any	
Nocturnal symptoms/awakening	None	Any	
Need for reliever/rescue treatment	None (twice or less/week)	More than twice/week	
Lung function (PEF or FEV_1)#	Normal	<80% predicted or personal best (if known)	
Exacerbations	None	One or more/year*	One in any week**

PEF = peak expiratory flow; FEV_1 = fraction of expired volume in 1 second

* Any exacerbation should prompt review of maintenance treatment to ensure that it is adequate.
** By definition, an exacerbation in any week makes that an uncontrolled asthma week.
# Lung function is not a reliable test for children 5 years and younger.

Treating to Achieve Control

The patient's current level of asthma control and current treatment determine the selection of pharmacologic treatment. For example, if asthma is not controlled on the current treatment regimen, treatment should be stepped up until control is achieved. If control has been maintained for at least three months, treatment can be stepped down with the aim of establishing the lowest step and dose of treatment that maintains control (see "Monitoring to Maintain Control," below.) If asthma is partly controlled, an increase in treatment should be considered, subject to whether more effective options are available (e.g., increased dose or an additional treatment), safety and cost of possible treatment options, and the patient's satisfaction with the level of control achieved. The scheme presented in Figure 4.3-2 in the original guideline document is based upon these principles, but the range and sequence of medications used in each clinical setting will vary depending on local availability (for cost or other reasons), acceptability, and preference.

Treatment Steps for Achieving Control

Step 1: As-Needed Reliever Medication

Step 1 treatment with an as-needed reliever medication is reserved for untreated patients with occasional daytime symptoms (cough, wheeze, dyspnea occurring twice or less per week, or less frequently if nocturnal) of short duration (lasting only a few hours) comparable with controlled asthma (see Table above). Between episodes, the patient is asymptomatic with normal lung function and there is no nocturnal awakening. When symptoms are more frequent, and/or worsen periodically, patients require regular controller treatment (see *Steps 2* or higher) in addition to as-needed reliever medication (**Evidence B**).

For the majority of patients in *Step 1*, a rapid-acting inhaled $beta_2$-agonist is the recommended reliever treatment (**Evidence A**). An inhaled anticholinergic, short-acting oral $beta_2$-agonist, or short-acting theophylline may be considered as alternatives, although they have a slower onset of action and higher risk of side effects (**Evidence A**).

Exercise-induced bronchoconstriction. Physical activity is an important cause of asthma symptoms for most asthma patients, and for some it is the only cause. However, exercise-induced bronchoconstriction often indicates that the patient's asthma is not well controlled, and stepping up controller therapy generally results in the reduction of exercise-related symptoms. For those patients who still experience exercise-induced bronchoconstriction despite otherwise well-controlled asthma, and for those in whom exercise-induced bronchoconstriction is the only manifestation of asthma, a rapid-acting inhaled $beta_2$-agonist (short- or long-acting), taken prior to exercise or to relieve symptoms that develop after exercise, is recommended. A leukotriene modifier or cromone are alternatives (**Evidence A**). Training and sufficient warm-up also reduce the incidence and severity of exercise-induced bronchoconstriction (**Evidence B**). Information on treatment of

exercise-induced asthma in athletes can be found in a Joint Task Force Report prepared by the European Respiratory Society, the European Academy of Allergy and Clinical Immunology, and GA(2)LEN and the World Anti-Doping Agency website (http://www.wada-ama.org).

Step 2: Reliever Medication Plus a Single Controller

Treatment *Steps 2* through *5*, combine an as-needed reliever treatment with regular controller treatment. At *Step 2*, a low-dose inhaled glucocorticosteroid is recommended as the initial controller treatment for asthma patients of all ages (**Evidence A**). Equivalent doses of inhaled glucocorticosteroids, some of which may be given as a single daily dose, are provided in Figure 3-1 in the original guideline document for adults and in Figure 3-4 in the original guideline document for children 5 years and younger.

Alternative controller medications include leukotriene modifiers (**Evidence A**), appropriate particularly for patients who are unable or unwilling to use inhaled glucocorticosteroids, or who experience intolerable side effects such as persistent hoarseness from inhaled glucocorticosteroid treatment and those with concomitant allergic rhinitis (**Evidence C**).

Other options are available but not recommended for routine use as initial or first-line controllers in *Step 2*. Sustained-release theophylline has only weak anti-inflammatory and controller efficacy (**Evidence B**) and is commonly associated with side effects that range from trivial to intolerable. Cromones (nedocromil sodium and sodium cromoglycate) have comparatively low efficacy, though a favorable safety profile (**Evidence A**).

Step 3: Reliever Medication Plus One or Two Controllers

At *Step 3*, the recommended option for adolescents and adults is to combine a low-dose of inhaled glucocorticosteroid with an inhaled long-acting $beta_2$-agonist, either in a combination inhaler device or as separate components (**Evidence A**). Because of the additive effect of this combination, the low-dose of glucocorticosteroid is usually sufficient, and need only be increased if control is not achieved within 3 or 4 months with this regimen (**Evidence A**). The long-acting $beta_2$-agonist formoterol, which has a rapid onset of action whether given alone or in combination inhaler with budesonide, has been shown to be as effective as short-acting $beta_2$-agonist in acute asthma exacerbation. However its use as monotherapy as a reliever medication is strongly discouraged since it must always be used in association with an inhaled glucocorticosteroid.

For all children but particularly those 5 years and younger, combination therapy has been less well studied and the addition of a long-acting beta agonist may not be as effective as increasing the dose of inhaled glucocorticosteroids in reducing exacerbations.

If a combination inhaler containing formoterol and budesonide is selected, it may be used for both rescue and maintenance. This approach has been shown to result in reductions in exacerbations and improvements in asthma control in adults and adolescents at relatively low doses of treatment (**Evidence A**). Whether this

approach can be employed with other combinations of controller and reliever requires further study.

Another option for both adults and children, but the one recommended for children, is to increase to a medium-dose of inhaled glucocorticosteroids (**Evidence A**). For patients of all ages on medium- or high-dose of inhaled glucocorticosteroid delivered by a pressurized metered-dose inhaler (MDI), use of a spacer device is recommended to improve delivery to the airways, reduce oropharyngeal side effects, and reduce systemic absorption (**Evidence A**).

Another option at *Step 3* is to combine a low-dose inhaled glucocorticosteroid with leukotriene modifiers (**Evidence A**). Alternatively, the use of sustained-release theophylline given at low-dose may be considered (**Evidence B**). These options have not been fully studied in children 5 years and younger.

Step 4: Reliever Medication Plus Two or More Controllers

The selection of treatment at *Step 4* depends on prior selections at *Steps 2* and *3*. However, the order in which additional medications should be added is based, as far as possible, upon evidence of their relative efficacy in clinical trials. Where possible, patients who are not controlled on *Step 3* treatments should be referred to a health professional with expertise in the management of asthma for investigation of alternative diagnoses and/or causes of difficult-to-treat asthma.

The preferred treatment at *Step 4* is to combine a medium- or high-dose of inhaled glucocorticosteroid with a long-acting inhaled $beta_2$-agonist. However, in most patients, the increase from a medium- to a high-dose of inhaled glucocorticosteroid provides relatively little additional benefit (**Evidence A**), and the high-dose is recommended only on a trial basis for 3 to 6 months when control cannot be achieved with medium-dose inhaled glucocorticosteroid combined with a long-acting $beta_2$-agonist and/or a third controller (e.g., leukotriene modifiers or sustained-release theophylline) (**Evidence B**). Prolonged use of high-dose inhaled glucocorticosteroids is also associated with increased potential for adverse effects. At medium- and high-doses, twice-daily dosing is necessary for most but not all inhaled glucocorticosteroids (**Evidence A**). With budesonide, efficacy may be improved with more frequent dosing (four times daily) (**Evidence B**). (Refer to Figure 3-1 in the original guideline document for adults and Figure 3-4 in the original guideline document for children 5 years and younger for recommendations on dosing and frequency for different inhaled glucocorticosteroids.)

Leukotriene modifiers as add-on treatment to medium-to high-dose inhaled glucocorticosteroids have been shown to provide benefit (**Evidence A**), but usually less than that achieved with the addition of a long-acting $beta_2$-agonist (**Evidence A**). The addition of a low-dose of sustained-release theophylline to medium- or high-dose inhaled glucocorticosteroid and long-acting $beta_2$-agonist may also provide benefit (**Evidence B**).

Step 5: Reliever Medication Plus Additional Controller Options

Addition of oral glucocorticosteroids to other controller medications may be effective (**Evidence D**) but is associated with severe side effects (**Evidence A**)

and should only be considered if the patient's asthma remains severely uncontrolled on *Step 4* medications with daily limitation of activities and frequent exacerbations. Patients should be counseled about potential side effects and all other alternative treatments must be considered.

Addition of anti-immunoglobulin E (anti-IgE) treatment to other controller medications has been shown to improve control of allergic asthma when control has not been achieved on combinations of other controllers including high-doses of inhaled or oral glucocorticosteroids (**Evidence A**).

Monitoring to Maintain Control

When asthma control has been achieved, ongoing monitoring is essential to maintain control and to establish the lowest step and dose of treatment necessary, which minimizes the cost and maximizes the safety of treatment. On the other hand, asthma is a variable disease, and treatment has to be adjusted periodically in response to loss of control as indicated by worsening symptoms or the development of an exacerbation.

Asthma control should be monitored by the health care professional and preferably also by the patient at regular intervals, using either a simplified scheme as presented in the Levels of Asthma Control table, above, or a validated composite measure of control. The frequency of health care visits and assessments depends upon the patient's initial clinical severity, and the patient's training and confidence in playing a role in the ongoing control of his or her asthma. Typically, patients are seen one to three months after the initial visit, and every three months thereafter. After an exacerbation, follow-up should be offered within two weeks to one month (**Evidence D**).

Duration and Adjustments to Treatment

For most classes of controller medications, improvement begins within days of initiating treatment, but the full benefit may only be evident after 3 or 4 months. In severe and chronically undertreated disease, this can take even longer.

The reduced need for medication once control is achieved is not fully understood, but may reflect the reversal of some of the consequences of long-term inflammation of the airways. Higher doses of anti-inflammatory medication may be required to achieve this benefit than to maintain it. Alternatively, the reduced need for medication might simply represent spontaneous improvement as part of the cyclical natural history of asthma. Rarely, asthma may go into remission particularly in children aged 5 years and younger and during puberty. Whatever the explanation, in all patients the minimum controlling dose of treatment must be sought through a process of regular follow-up and staged dose reductions.

At other times treatment may need to be increased either in response to loss of control or threat of loss of control (return of symptoms) or an acute exacerbation, which is defined as a more acute and severe loss of control that requires urgent treatment. (An approach to exacerbations is provided in Component 4 below.)

Stepping Down Treatment When Asthma Is Controlled

There is little experimental data on the optimal timing, sequence, and magnitude of treatment reductions in asthma, and the approach will differ from patient to patient depending on the combination of medications and the doses that were needed to achieve control. These changes should ideally be made by agreement between patient and health care professional, with full discussion of potential consequences including reappearance of symptoms and increased risk of exacerbations.

Although further research on stepping down asthma treatment is needed, some recommendations can be made based on the current evidence:

- When inhaled glucocorticosteroids alone in medium-to-high-doses are being used, a 50% reduction in dose should be attempted at 3 month intervals (**Evidence B**).
- Where control is achieved at a low-dose of inhaled glucocorticosteroids alone, in most patients treatment may be switched to once-daily dosing (**Evidence A**).
- When asthma is controlled with a combination of inhaled glucocorticosteroid and long-acting $beta_2$-agonist, the preferred approach is to begin by reducing the dose of inhaled glucocorticosteroid by approximately 50% while continuing the long-acting $beta_2$-agonist (**Evidence B**). If control is maintained, further reductions in the glucocorticosteroid should be attempted until a low-dose is reached, when the long-acting $beta_2$-agonist may be stopped (**Evidence D**). An alternative is to switch the combination treatment to once-daily dosing. A second alternative is to discontinue the long-acting $beta_2$-agonist at an earlier stage and substitute the combination treatment with inhaled glucocorticosteroid monotherapy at the same dose contained in the combination inhaler. However, for some patients these alternative approaches lead to loss of asthma control (**Evidence B**).
- When asthma is controlled with inhaled glucocorticosteroids in combination with controllers other than long-acting $beta_2$-agonists, the dose of inhaled glucocorticosteroid should be reduced by 50% until a low-dose of inhaled glucocorticosteroid is reached, then the combination treatment stopped as described above (**Evidence D**).
- Controller treatment may be stopped if the patient's asthma remains controlled on the lowest dose of controller and no recurrence of symptoms occurs for one year (**Evidence D**).

Stepping Up Treatment In Response To Loss Of Control

Treatment has to be adjusted periodically in response to worsening control, which may be recognized by the minor recurrence or worsening of symptoms. Treatment options are as follows:

- Rapid-onset, short-acting or long-acting $beta_2$-agonist bronchodilators. Repeated dosing with bronchodilators in this class provides temporary relief until the cause of the worsening symptoms passes. The need for repeated doses over more than one or two days signals the need for review and possible increase of controller therapy.
- Inhaled glucocorticosteroids. Temporarily doubling the dose of inhaled glucocorticosteroids has not been demonstrated to be effective, and is no longer recommended (**Evidence A**). A four-fold or greater increase has been

demonstrated to be equivalent to a short course of oral glucocorticosteroids in adult patients with an acute deterioration (**Evidence A**). The higher dose should be maintained for seven to fourteen days but more research is needed in both adults and children to standardize the approach.

- Combination of inhaled glucocorticosteroids and rapid and long-acting $beta_2$-agonist bronchodilator (e.g., formoterol) for combined relief and control. The use of the combination of a rapid and long-acting $beta_2$-agonist and an inhaled glucocorticosteroid in a single inhaler both as a controller and reliever is effective in maintaining a high level of asthma control and reduces exacerbations requiring systemic glucocorticosteroids and hospitalization (**Evidence A**). The benefit in preventing exacerbations appears to be the consequence of early intervention at a very early stage of a threatened exacerbation since studies involving doubling or quadrupling doses of combination treatment once deterioration is established (for 2 or more days) show some benefit but results are inconsistent. Because there are no studies using this approach with other combinations of controller and relievers, other than budesonide/formoterol, the alternative approaches described in this section should be used for patients on other controller therapies. Combination therapy with budesonide and formoterol used both as maintenance and rescue has been shown to reduce asthma exacerbations in children ages 4 years and older with moderate to severe asthma.
- The usual treatment for an acute exacerbation is a high-dose of $beta_2$-agonist and a burst of systemic glucocorticosteroids administered orally or intravenously. (Refer to Component 4 below for more information.)

Following treatment for an exacerbation of asthma, maintenance treatment can generally be resumed at previous levels unless the exacerbation was associated with a gradual loss of control suggesting chronic undertreatment. In this case, provided inhaler technique has been checked, a step-wise increase in treatment (either in dose or number of controllers) is indicated.

Difficult-to-Treat Asthma

Although the majority of asthma patients can obtain the targeted level of control, some patients will not do so even with the best therapy. Patients who do not reach an acceptable level of control at *Step 4* (reliever medication plus two or more controllers) can be considered to have difficult-to-treat asthma. These patients may have an element of poor glucocorticosteroid responsiveness, and require higher doses of inhaled glucocorticosteroids than are routinely used in patients whose asthma is easy to control. However, there is currently no evidence to support continuing these high doses of inhaled glucocorticosteroids beyond 6 months in the hope of achieving better control. Instead, dose optimization should be pursued by stepping down to a dose that maintains the maximal level of control achieved on the higher dose.

Because very few patients are completely resistant to glucocorticosteroids, these medications remain a mainstay of therapy for difficult-to-treat asthma, while additional diagnostic and generalized therapeutic options can and should also be considered:

- Confirm the diagnosis of asthma. In particular, the presence of chronic obstructive pulmonary disease (COPD) must be excluded. Vocal cord dysfunction must be considered.
- Investigate and confirm compliance with treatment. Incorrect or inadequate use of medications remains the most common reason for failure to achieve control.
- Consider smoking, current or past, and encourage complete cessation. A history of past tobacco smoking is associated with a reduced likelihood of complete asthma control, and this is only partly attributable to the presence of fixed airflow obstruction. In addition, current smoking reduces the effectiveness of inhaled and oral glucocorticosteroids. Counseling and smoking cessation programs should be offered to all asthma patients who smoke.
- Investigate the presence of comorbidities that may aggravate asthma. Chronic sinusitis, gastroesophageal reflux, and obesity/obstructive sleep apnea have been reported in higher percentages in patients with difficult-to-treat asthma. Psychological and psychiatric disorders should also be considered. If found, these comorbidities should be addressed and treated as appropriate, although the ability to improve asthma control by doing so remains unconfirmed.

When these reasons for lack of treatment response have been considered and addressed, a compromise level of control may need to be accepted and discussed with the patient to avoid futile over-treatment (with its attendant cost and potential for adverse effects). The objective is then to minimize exacerbations and need for emergency medical interventions while achieving as high a level of clinical control with as little disruption of activities and as few daily symptoms as possible. For these difficult-to-treat patients, frequent use of rescue medication is accepted, as is a degree of chronic lung function impairment.

Although lower levels of control are generally associated with an increased risk of exacerbations, not all patients with chronically impaired lung function, reduced activity levels, and daily symptoms have frequent exacerbations. In such patients, the lowest level of treatment that retains the benefits achieved at the higher doses of treatment should be employed. Reductions should be made cautiously and slowly at intervals not more frequent than 3 to 6 months, as carryover of the effects of the higher dose may last for several months and make it difficult to assess the impact of the dose reduction (**Evidence D**). Referral to a physician with an interest in and/or special focus on asthma may be helpful and patients may benefit from phenotyping into categories such as allergic, aspirin-sensitive, and/or eosinophilic asthma. Patients categorized as allergic might benefit from anti-IgE therapy, and leukotriene modifiers can be helpful for patients determined to be aspirin sensitive (who are often eosinophilic as well).

Component 4: Manage Asthma Exacerbations

Key Points

- Exacerbations of asthma (asthma attacks or acute asthma) are episodes of progressive increase in shortness of breath, cough, wheezing, or chest tightness, or some combination of these symptoms.
- Exacerbations are characterized by decreases in expiratory airflow that can be

quantified and monitored by measurement of lung function (peak expiratory flow rate [PEF] or forced expiratory volume in one second [FEV_1]).
- The primary therapies for exacerbations include the repetitive administration of rapid-acting inhaled bronchodilators, the early introduction of systemic glucocorticosteroids, and oxygen supplementation.
- The aims of treatment are to relieve airflow obstruction and hypoxemia as quickly as possible, and to plan the prevention of future relapses.
- Severe exacerbations are potentially life threatening, and their treatment requires close supervision. Most patients with severe asthma exacerbations should be treated in an acute care facility. Patients at high risk of asthma-related death also require closer attention.
- Milder exacerbations, defined by a reduction in peak flow of less than 20%, nocturnal awakening, and increased use of short acting $beta_2$-agonists can usually be treated in a community setting.

Introduction

Exacerbations of asthma (asthma attacks or acute asthma) are episodes of progressive increase in shortness of breath, cough, wheezing, or chest tightness, or some combination of these symptoms. Exacerbations usually have a progressive onset but a subset of patients (mostly adults) present more acutely. Respiratory distress is common. Exacerbations are characterized by decreases in expiratory airflow that can be quantified by measurement of lung function (PEF or FEV_1). These measurements are more reliable indicators of the severity of airflow limitation than is the degree of symptoms. The degree of symptoms may, however, be a more sensitive measure of the onset of an exacerbation because the increase in symptoms usually precedes the deterioration in peak flow rate. Still, a minority of patients perceive symptoms poorly, and may have a significant decline in lung function without a significant change in symptoms. This situation especially affects patients with a history of near-fatal asthma and also appears to be more likely in males. A clinically useful tool to assess the likelihood of asthma-related hospitalizations or emergency department visits in adults with severe or difficult to treat asthma has been described.

Strategies for treating exacerbations, though generalizable, are best adapted and implemented at a local level. Severe exacerbations are potentially life threatening, and their treatment requires close supervision. Patients with severe exacerbations should be encouraged to see their physician promptly or, depending on the organization of local health services, to proceed to the nearest clinic or hospital that provides emergency access for patients with acute asthma. Close objective monitoring (PEF) of the response to therapy is essential.

The primary therapies for exacerbations include—in the order in which they are introduced, depending on severity—repetitive administration of rapid-acting inhaled bronchodilators, early introduction of systemic glucocorticosteroids, and oxygen supplementation. The aims of treatment are to relieve airflow obstruction and hypoxemia as quickly as possible, and to plan the prevention of future relapses.

Patients at high risk of asthma-related death require closer attention and should be encouraged to seek urgent care early in the course of their exacerbations. These patients include those:

- With a history of near-fatal asthma requiring intubation and mechanical ventilation
- Who have had a hospitalization or emergency care visit for asthma in the past year
- Who are currently using or have recently stopped using oral glucocorticosteroids
- Who are not currently using inhaled glucocorticosteroids
- Who are overdependent on rapid-acting inhaled $beta_2$-agonists, especially those who use more than one canister of salbutamol (or equivalent) monthly
- With a history of psychiatric disease or psychosocial problems, including the use of sedatives
- With a history of noncompliance with an asthma medication plan

Response to treatment may take time and patients should be closely monitored using clinical as well as objective measurements. The increased treatment should continue until measurements of lung function (PEF or FEV_1) return to their previous best (ideally) or plateau, at which time a decision to admit or discharge can be made based upon these values. Patients who can be safely discharged will have responded within the first two hours, at which time decisions regarding patient disposition can be made.

Assessment of Severity

The severity of the exacerbation (see Figure 4.4-1 in the original guideline document) determines the treatment administered. Indices of severity, particularly PEF (in patients older than 5 years), pulse rate, respiratory rate, and pulse oximetry, should be monitored during treatment.

Management—Community Settings

Most patients with severe asthma exacerbations should be treated in an acute care facility (such as a hospital emergency department) where monitoring, including objective measurement of airflow obstruction, oxygen saturation, and cardiac function, is possible. Milder exacerbations, defined by a reduction in peak flow of less than 20%, nocturnal awakening, and increased use of short acting $beta_2$-agonists can usually be treated in a community setting. If the patient responds to the increase in inhaled bronchodilator treatment after the first few doses, referral to an acute care facility is not required, but further management under the direction of a primary care physician may include the use of systemic glucocorticosteroids. Patient education and review of maintenance therapy should also be undertaken.

Treatment

<u>Bronchodilators</u>

For mild to moderate exacerbations, repeated administration of rapid-acting inhaled $beta_2$-agonists (2 to 4 puffs every 20 minutes for the first hour) is usually the best and most cost-effective method of achieving rapid reversal of airflow limitation. After the first hour, the dose of $beta_2$-agonist required will depend on the severity of the exacerbation. Mild exacerbations respond to 2 to 4 puffs every 3 to 4 hours; moderate exacerbations will require 6 to 10 puffs every 1 or 2 hours. Treatment should also be titrated depending upon the individual patient's response, and if there is a lack of response or other concern about how the patient is responding, the patient should be referred to an acute care facility.

Many patients will be able to monitor their PEF after the initiation of increased bronchodilator therapy. Bronchodilator therapy delivered via an MDI, ideally with a spacer, produces at least an equivalent improvement in lung function as the same dose delivered via nebulizer. At the clinic level, this route of delivery is the most cost effective, provided patients are able to use an MDI. No additional medication is necessary if the rapid-acting inhaled $beta_2$-agonist produces a complete response (PEF returns to greater than 80% of predicted or personal best) and the response lasts for 3 to 4 hours.

Glucocorticosteroids

Oral glucocorticosteroids (0.5 to 1 mg of prednisolone/kg or equivalent during a 24-hour period) should be used to treat exacerbations, especially if they develop after instituting the other short-term treatment options recommended for loss of control (see "Stepping up treatment in response to loss of control" in Component 3 above and in the original guideline document). If patients fail to respond to bronchodilator therapy, as indicated by persistent airflow obstruction, prompt transfer to an acute care setting is recommended, especially if they are in a high risk group.

Management—Acute Care Settings

Severe exacerbations of asthma are life-threatening medical emergencies, treatment of which is often most safely undertaken in an emergency department. The algorithm in Figure 4.4-2 in the original guideline document illustrates the approach to acute care-based management of exacerbations.

Assessment

A brief history and physical examination pertinent to the exacerbation should be conducted concurrently with the prompt initiation of therapy. The history should include severity and duration of symptoms, including exercise limitation and sleep disturbance; all current medications, including dose (and device) prescribed, dose usually taken, dose taken in response to the deterioration, and the patient's response (or lack thereof) to this therapy; time of onset and cause of the present exacerbation; and risk factors for asthma-related death.

The physical examination should assess exacerbation severity by evaluating the patient's ability to complete a sentence, pulse rate, respiratory rate, use of accessory muscles, and other signs detailed in Figure 4.4-2 in the original guideline document. Any complicating factors should be identified (e.g., pneumonia, atelectasis, pneumothorax, or pneumomediastinum).

Functional assessments such as PEF or FEV_1 and arterial oxygen saturation measurements are strongly recommended as physical examination alone may not fully indicate the severity of the exacerbation, particularly the degree of hypoxemia. Without unduly delaying treatment, a baseline PEF or FEV_1 measurement should be made before treatment is initiated. Subsequent measurements should be made at intervals until a clear response to treatment has occurred.

Oxygen saturation should be closely monitored, preferably by pulse oximetry. This is especially useful in children because objective measurements of lung function may be difficult. Oxygen saturation in children should normally be greater than 95%, and oxygen saturation less than 92% is a good predictor of the need for hospitalization (**Evidence C**).

In adults a chest x-ray is not routinely required, but should be carried out if a complicating cardiopulmonary process is suspected, in patients requiring hospitalization, and in those not responding to treatment where a pneumothorax may be difficult to diagnose clinically. Similarly, in children routine chest x-rays are not recommended unless there are physical signs suggestive of parenchymal disease.

Although arterial blood gas measurements are not routinely required, they should be completed in patients with a PEF of 30 to 50% predicted, those who do not respond to initial treatment, or when there is concern regarding deterioration. The patient should continue on supplemental oxygen while the measurement is made. A partial pressure of oxygen in arterial blood (PaO_2) <60 mm Hg (8 kPa) and a normal or increased partial pressure of carbon dioxide in the arterial blood ($PaCO_2$) (especially >45 mm Hg, 6 kPa) indicates the presence of respiratory failure.

Treatment

The following treatments are usually administered concurrently to achieve the most rapid resolution of the exacerbation:

Oxygen

To achieve arterial oxygen saturation of ≥90% (≥95% in children), oxygen should be administered by nasal cannulae, by mask, or rarely by head box in some infants. $PaCO_2$ may worsen in some patients on 100 percent oxygen, especially those with more severe airflow obstruction. Oxygen therapy should be titrated against pulse oximetry to maintain a satisfactory oxygen saturation.

Rapid-Acting Inhaled $Beta_2$–Agonists

Rapid-acting inhaled $beta_2$-agonists should be administered at regular intervals (**Evidence A**). Although most rapid-acting $beta_2$-agonists have a short duration of effect, the long-acting bronchodilator formoterol, which has both a rapid onset of action and a long duration of effect, has been shown to be equally effective without increasing side effects, though it is considerably more expensive. The importance of this feature of formoterol is that it provides support and

reassurance regarding the use of a combination of formoterol and budesonide early in asthma exacerbations.

A modestly greater bronchodilator effect has been shown with levalbuterol compared to racemic albuterol in both adults and children with an asthma exacerbation. In a large study of acute asthma in children, and in adults not previously treated with glucocorticosteroids, levalbuterol treatment resulted in lower hospitalization rates compared to racemic albuterol treatment, but in children the length of hospital stay was no different.

A reasonable approach to inhaled therapy in exacerbations would be the initial use of continuous therapy, followed by intermittent on-demand therapy for hospitalized patients. There is no evidence to support the routine use of intravenous beta$_2$-agonists in patients with severe asthma exacerbations.

Epinephrine

A subcutaneous or intramuscular injection of epinephrine (adrenaline) may be indicated for acute treatment of anaphylaxis and angioedema, but is not routinely indicated during asthma exacerbations.

Additional Bronchodilators

Ipratropium bromide. A combination of nebulized beta$_2$- agonist with an anticholinergic (ipratropium bromide) may produce better bronchodilation than either drug alone (**Evidence B**) and should be administered before methylxanthines are considered. Combination beta$_2$-agonist/anticholinergic therapy is associated with lower hospitalization rates (**Evidence A**) and greater improvement in PEF and FEV$_1$ (**Evidence B**). Similar data have been reported in the pediatric literature (**Evidence A**). However, once children with asthma are hospitalized following intensive emergency department treatment, the addition of nebulized ipratropium bromide to nebulized beta$_2$-agonist and systemic glucocorticosteroids appears to confer no extra benefit.

Theophylline. In view of the effectiveness and relative safety of rapid-acting beta$_2$-agonists, theophylline has a minimal role in the management of acute asthma. Its use is associated with severe and potentially fatal side effects, particularly in those on long-term therapy with sustained-release theophylline, and their bronchodilator effect is less than that of beta$_2$-agonists. The benefit as add-on treatment in adults with severe asthma exacerbations has not been demonstrated. However, in one study of children with near-fatal asthma, intravenous theophylline provided additional benefit to patients also receiving an aggressive regimen of inhaled and intravenous beta$_2$-agonists, inhaled ipratropium bromide, and intravenous systemic glucocorticosteroids.

Systemic Glucocorticosteroids

Systemic glucocorticosteroids speed resolution of exacerbations and should be utilized in the all but the mildest exacerbations (**Evidence A**), especially if:

- The initial rapid-acting inhaled beta$_2$-agonist therapy fails to achieve lasting improvement
- The exacerbation develops even though the patient was already taking oral glucocorticosteroids
- Previous exacerbations required oral glucocorticosteroids

Oral glucocorticosteroids are usually as effective as those administered intravenously and are preferred because this route of delivery is less invasive and less expensive. If vomiting has occurred shortly after administration of oral glucocorticosteroids, then an equivalent dose should be re-administered intravenously. In patients discharged from the emergency department, intramuscular administration may be helpful, especially if there are concerns about compliance with oral therapy. Oral glucocorticosteroids require at least 4 hours to produce clinical improvement. Daily doses of systemic glucocorticosteroids equivalent to 60-80 mg methylprednisolone as a single dose, or 300-400 mg hydrocortisone in divided doses, are adequate for hospitalized patients, and 40 mg methylprednisolone or 200 mg hydrocortisone is probably adequate in most cases (**Evidence B**). An oral glucocorticosteroid dose of 1 mg/kg daily is adequate for treatment of exacerbations in children with mild persistent asthma. A 7-day course in adults has been found to be as effective as a 14-day course, and a 3- to 5-day course in children is usually considered appropriate (**Evidence B**). Current evidence suggests that there is no benefit to tapering the dose of oral glucocorticosteroids, either in the short-term or over several weeks (**Evidence B**).

Inhaled Glucocorticosteroids

Inhaled glucocorticosteroids are effective as part of therapy for asthma exacerbations. In one study, the combination of high-dose inhaled glucocorticosteroids and salbutamol in acute asthma provided greater bronchodilation than salbutamol alone (**Evidence B**), and conferred greater benefit than the addition of systemic glucocorticosteroids across all parameters, including hospitalizations, especially for patients with more severe attacks.

Inhaled glucocorticosteroids can be as effective as oral glucocorticosteroids at preventing relapses. Patients discharged from the emergency department on prednisone and inhaled budesonide have a lower rate of relapse than those on prednisone alone (**Evidence B**). A high dose of inhaled glucocorticosteroid (2.4 mg budesonide daily in four divided doses) achieves a relapse rate similar to 40 mg oral prednisone daily (**Evidence A**). Cost is a significant factor in the use of such high-doses of inhaled glucocorticosteroids, and further studies are required to document their potential benefits, especially cost effectiveness, in acute asthma.

Magnesium

Intravenous magnesium sulphate (usually given as a single 2 g infusion over 20 minutes) is not recommended for routine use in asthma exacerbations, but can help reduce hospital admission rates in certain patients, including adults with FEV_1 25-30% predicted at presentation, adults and children who fail to respond to initial treatment, and children whose FEV_1 fails to improve above 60% predicted after 1 hour of care (**Evidence A**). Nebulized salbutamol administered in isotonic

magnesium sulfate provides greater benefit than if it is delivered in normal saline (**Evidence A**). Intravenous magnesium sulphate has not been studied in young children.

Helium Oxygen Therapy

A systematic survey of studies that have evaluated the effect of a combination of helium and oxygen, compared to helium alone, suggests there is no routine role for this intervention. It might be considered for patients who do not respond to standard therapy.

Leukotriene Modifiers

There is little data to suggest a role for leukotriene modifiers in acute asthma.

Sedatives

Sedation should be strictly avoided during exacerbations of asthma because of the respiratory depressant effect of anxiolytic and hypnotic drugs. An association between the use of these drugs and avoidable asthma deaths has been demonstrated.

Criteria for Discharge from the Emergency Department vs. Hospitalization

Patients with a pre-treatment FEV_1 or PEF <25% predicted or personal best, or those with a post-treatment FEV_1 or PEF <40% predicted or personal best, usually require hospitalization. Patients with post-treatment lung function of 40 to 60% predicted may be discharged, provided that adequate follow-up is available in the community and compliance is assured. Patients with post-treatment lung function ≥60% predicted can be discharged.

Management of acute asthma in the intensive care unit is beyond the scope of this document and readers are referred to recent comprehensive reviews.

For patients discharged from the emergency department:

- At a minimum, a 7-day course of oral glucocorticosteroids for adults and a shorter course (3 to 5 days) for children should be prescribed, along with continuation of bronchodilator therapy.
- The bronchodilator can be used on an as-needed basis, based on both symptomatic and objective improvement, until the patient returns to his or her pre-exacerbation use of rapid-acting inhaled $beta_2$-agonists.
- Ipratropium bromide is unlikely to provide additional benefit beyond the acute phase and may be quickly discontinued.
- Patients should initiate or continue inhaled glucocorticosteroids.
- The patient's inhaler technique and use of peak flow meter to monitor therapy at home should be reviewed. Patients discharged from the emergency department with a peak flow meter and action plan have a better response than patients discharged without these resources.
- The factors that precipitated the exacerbation should be identified and strategies for their future avoidance implemented.

- The patient's response to the exacerbation should be evaluated. The action plan should be reviewed and written guidance provided.
- Use of controller therapy during the exacerbation should be reviewed: whether this therapy was increased promptly, by how much, and, if appropriate, why oral glucocorticosteroids were not added. Consider providing a short course of oral glucocorticosteroids to be on hand for subsequent exacerbations.
- The patient or family should be instructed to contact the primary health care professional or asthma specialist within 24 hours of discharge. A follow-up appointment with the patient's usual primary care professional or asthma specialist should be made within a few days of discharge to assure that treatment is continued until baseline control parameters, including personal best lung function, are reached. Prospective data indicate that patients discharged from the emergency department for follow-up with specialist care do better that patients returned to routine care.

An exacerbation severe enough to require hospitalization may reflect a failure of the patient's self-management plan. Hospitalized patients may be particularly receptive to information and advice about their illness. Health care providers should take the opportunity to review patient understanding of the causes of asthma exacerbations, avoidance of factors that may cause exacerbations (including, where relevant smoking cessation), the purposes and correct uses of treatment, and the actions to be taken to respond to worsening symptoms or peak flow values (**Evidence A**).

Referral to an asthma specialist should be considered for hospitalized patients. Following discharge from continuous supervision, the patient should be reviewed by the family health care professional or asthma specialist regularly over the subsequent weeks until personal best lung function is reached. Use of incentives improves primary care follow up but has shown no effect on long term outcomes. Patients who come to the emergency department with an acute exacerbation should be especially targeted for an asthma education program, if one is available.

Component 5: Special Considerations

Pregnancy

Inhaled glucocorticosteroids have been shown to prevent exacerbations of asthma during pregnancy (Evidence B). As in other situations, the focus of asthma treatment must remain on control of symptoms and maintenance of normal lung function. Acute exacerbations should be treated aggressively in order to avoid fetal hypoxia. Treatment should include nebulized rapid-acting $beta_2$-agonists and oxygen and systemic glucocorticosteroids should be instituted when necessary.

While all patients should have adequate opportunity to discuss the safety of their medications, pregnant patients with asthma should be advised that the greater risk to their baby lies with poorly controlled asthma, and the safety of most modern asthma treatments should be stressed. Even with a good patient/health care professional relationship, independent printed material, such as a statement from the US National Asthma Education and Prevention Program on the treatment of asthma during pregnancy, will provide important additional reassurance.

Surgery

Airway hyperresponsiveness, airflow limitation, and mucus hypersecretion predispose patients with asthma to intraoperative and postoperative respiratory complications. The likelihood of these complications depends on the severity of asthma at the time of surgery, the type of surgery (thoracic and upper abdominal surgeries pose the greatest risks), and type of anesthesia (general anesthesia with endotracheal intubation carries the greatest risk). These variables need to be assessed prior to surgery and pulmonary function should be measured. If possible, this evaluation should be undertaken several days before surgery to allow time for additional treatment. In particular, if the patient's FEV_1 is less than 80% of personal best, a brief course of oral glucocorticosteroids should be considered to reduce airflow limitation (**Evidence C**). Furthermore, patients who have received systemic glucocorticosteroids within the past 6 months should have systemic coverage during the surgical period (100 mg hydrocortisone every 8 hours intravenously). This should be rapidly reduced 24 hours following surgery, as prolonged systemic glucocorticosteroid therapy may inhibit wound healing (**Evidence C**).

Rhinitis

Treatment of rhinitis may improve asthma symptoms (**Evidence A**). Anti-inflammatory agents including glucocorticosteroids and cromones as well as leukotriene modifiers and anticholinergics can be effective in both conditions. However, some medications are selectively effective against rhinitis (e.g., H_1-antagonists) and others against asthma (e.g., $beta_2$-agonists) (**Evidence A**). Use of intra-nasal glucocorticosteroids for concurrent rhinitis has been found to have a limited benefit in improving asthma and reducing asthma morbidity in some but not all studies. Leukotriene modifiers, allergen-specific immunotherapy, and anti-IgE therapy are effective in both conditions (**Evidence A**).

Sinusitis

Sinusitis is a complication of upper respiratory infections, allergic rhinitis, nasal polyps, and other forms of nasal obstruction. Both acute and chronic sinusitis can worsen asthma. Clinical features of sinusitis lack diagnostic precision, and computed tomography (CT) scan confirmation is recommended when available. In children with suspected rhinosinusitis, antibiotic therapy for 10 days is recommended (**Evidence B**). Treatment should also include medications to reduce nasal congestion, such as topical nasal decongestants or topical nasal or even systemic glucocorticosteroids. These agents remain secondary to primary asthma therapies.

Occupational Asthma

Pharmacologic therapy for occupational asthma is identical to therapy for other forms of asthma, but it is not a substitute for adequate avoidance. Consultation with a specialist in asthma management or occupational medicine is advisable.

Respiratory Infections

Treatment of an infectious exacerbation follows the same principles as treatment of other asthma exacerbations—that is, rapid-acting inhaled $beta_2$-agonists and early introduction of oral glucocorticosteroids or increases in inhaled glucocorticosteroids by at least four-fold are recommended. Because increased asthma symptoms can often persist for weeks after the infection is cleared, anti-inflammatory treatment should be continued for this full period to ensure adequate control.

Aspirin-Induced Asthma (AIA)

A characteristic history of reaction is considered adequate for initiating avoidance strategies. However, the diagnosis can only be confirmed by aspirin challenge, as there are no suitable in vitro tests for diagnosis. The aspirin challenge test is not recommended for routine practice as it is associated with a high risk of potentially fatal consequences and must only be conducted in a facility with cardiopulmonary resuscitation capabilities. Further safeguards are that patients should only be challenged when their asthma is in remission and their FEV_1 is greater than 70% of predicted or personal best. Bronchial (inhalational) and nasal challenges with lysine aspirin are safer than oral challenges and may be performed in specialized centers. Once aspirin or NSAID hypersensitivity develops, it is present for life. Patients with AIA should avoid aspirin, products containing it, other analgesics that inhibit COX-1, and often also hydrocortisone hemisuccinate. Avoidance does not prevent progression of the inflammatory disease of the respiratory tract. Where a nonsteroidal anti-inflammatory drug (NSAID) is indicated, a cyclooxygenase-2 (COX-2) inhibitor may be considered with appropriate physician supervision and observation for at least one hour after administration (**Evidence B**). Glucocorticosteroids continue to be the mainstay of asthma therapy, but leukotriene modifiers may also be useful for additional control of the underlying disease (**Evidence B**). For NSAID-sensitive patients with asthma who require NSAIDs for other medical conditions, desensitization may be conducted in the hospital under the care of a specialist.

Special considerations are required in managing asthma in relation to pregnancy; surgery; rhinitis, sinusitis, and nasal polyps; occupational asthma; respiratory infections; gastroesophageal reflux; aspirin-induced asthma; and anaphylaxis. See the original guideline document for a detailed discussion of these special considerations.

Definitions:

Evidence Category	Sources of Evidence	Definition
A	Randomized controlled trials (RCTs). Rich body of data	Evidence is from endpoints of well-designed RCTs that provide a consistent pattern of findings in the population for which the recommendation is made. Category A requires substantial numbers of studies involving

Evidence Category	Sources of Evidence	Definition
		substantial numbers of participants.
B	Randomized controlled trials. Limited body of data.	Evidence is from endpoints of intervention studies that include only a limited number of patients, post hoc or subgroup analysis of RCTs, or meta-analysis of RCTs. In general, Category B pertains when few randomized trials exist, they are small in size, they were undertaken in a population that differs from the target population of the recommendation, or the results are somewhat inconsistent.
C	Nonrandomized trials. Observational studies.	Evidence is from outcomes of uncontrolled or nonrandomized trials or from observational studies.
D	Panel consensus judgment.	This category is used only in cases where the provision of some guidance was deemed valuable but the clinical literature addressing the subject was deemed insufficient to justify placement in one of the other categories. The Panel Consensus is based on clinical experience or knowledge that does not meet the above-listed criteria.

CLINICAL ALGORITHM(S)

Algorithms are provided in the original guideline document for:

- Management Approach Based On Control
- Management of Asthma Exacerbations in Acute Care Setting

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for select recommendations (see "Major Recommendations" field).

The recommendations on asthma management and prevention are based as far as possible on controlled clinical studies. For those aspects of the clinical management of asthma that have not been the subject of specific clinical studies, recommendations are based on literature review, clinical experience, and expert opinion of project members.

Levels of evidence are assigned to management recommendations in the Global Initiative for Asthma documents where appropriate in Chapter 4, the Five Components of Asthma Management. Evidence levels are indicated in boldface type enclosed in parentheses after the relevant statement—e.g., (**Evidence A**). The methodological issues concerning the use of evidence from meta-analyses were carefully considered.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- There is now good evidence that the clinical manifestations of asthma—symptoms, sleep disturbances, limitations of daily activity, impairment of lung function, and use of rescue medications—can be controlled with appropriate treatment.
- Although there is no cure for asthma, appropriate management that includes a partnership between the physician and the patient/family most often results in the achievement of control.
- The goals for successful management of asthma are to:
    - Achieve and maintain control of symptoms
    - Maintain normal activity levels, including exercise
    - Maintain pulmonary function as close to normal as possible
    - Prevent asthma exacerbations
    - Avoid adverse effects from asthma medications
    - Prevent asthma mortality

POTENTIAL HARMS

See Chapter 3 "Asthma Treatments" in the original guideline document for a full discussion of asthma medications for adults and children, including their side effects.

CONTRAINDICATIONS

CONTRAINDICATIONS

Sedation is contraindicated in the treatment of an asthma exacerbation.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

A large segment of the world's population lives in areas with inadequate medical facilities and meager financial resources. The Global Initiative for Asthma Executive Committee recognizes that "fixed" international guidelines and "rigid" scientific protocols will not work in many locations. Thus, the recommendations found in this Report must be adapted to fit local practices and the availability of health care resources.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Key Points

- In order to effect changes in medical practice and consequent improvements in patient outcomes, evidence-based guidelines must be implemented and disseminated at the national and local levels.
- Implementation of asthma guidelines should involve a wide variety of professional groups and other stakeholders, and take into account local cultural and economic conditions.
- An important part of the implementation process is to establish a system to evaluate the effectiveness and quality of care.
- Those involved in the adaptation and implementation of asthma guidelines require an understanding of the cost and cost effectiveness of various management recommendations in asthma care.
- Global Initiative for Asthma (GINA) has developed a number of resources and programs to aid in guideline implementation and dissemination.

It has been demonstrated in a variety of settings that patient care consistent with recommendations in evidence-based asthma guidelines leads to improved outcomes. Guidelines are designed to ensure that all members of a patient's health care team are aware of the goals of treatment and of the different ways of achieving these goals. They help set standards of clinical care, may serve as a basis for audit and payment, and act as a starting point for the education of health professionals and patients.

However, in order to effect changes in medical practice and consequent improvements in patient outcomes, evidence-based guidelines must be implemented and disseminated at national and local levels. Dissemination involves educating clinicians to improve their awareness, knowledge, and understanding of guideline recommendations. It is one part of implementation, which involves the translation of evidence-based asthma guidelines into real-life practice with improvement of health outcomes for the patient. Implementation remains a difficult problem worldwide. Barriers to implementation range from poor infrastructure that hampers delivery of medicines to remote parts of a country, to cultural factors that make patients reluctant to use recommended medications

(e.g., inhaled preparations), suboptimal use of medications, and lack of physician use of guidelines. An important barrier to the successful translation of asthma guidelines into clinical practice is access to available and affordable medication especially for patients in less developed economies where the cost of treatment is high in comparison to income and assets.

Guideline Implementation Strategies

Implementation of asthma guidelines should begin with the setting of goals and development of strategies for asthma care through collaboration among diverse professional groups including both primary and secondary health care professionals, public health officials, patients, asthma advocacy groups, and the general public. Goals and implementation strategies will vary from country to country–and within countries–for reasons of economics, culture, and environment. However, common issues are shown in Figure 5-1 in the original guideline document.

The next step is adaptation of guidelines on asthma management for local use by teams of local primary and secondary care health professionals. Many low- and middle income countries do not consider asthma a high-priority health concern because other, more common respiratory diseases such as tuberculosis and pneumonia are of greater public health importance. Therefore, practical asthma guidelines for implementation in low-income countries should have a simple algorithm for separating non-infectious from infectious respiratory illnesses; simple objective measurements for diagnosis and management such as peak flow variability; available, affordable, and low-risk medications recommended for asthma control; a simple regime for recognizing severe asthma; and simple diagnosis an management approaches relevant to the facilities and limited resources available.

Next, adapted guidelines must be widely disseminated in multiple venues and using multiple formats. This can be accomplished, for example, by publication in professional journals, accompanied by multidisciplinary symposia, workshops, and conferences involving national and local experts with involvement of the professional and mass media to raise awareness of the key messages. The most effective interventions to improve professional practice are multifaceted and interactive. However, little is known of the cost effectiveness of these interventions. Integrated care pathways are being explored as a mean to improve asthma care in specific settings, such as patients coming to emergency departments.

In some countries, implementation of asthma guidelines has been done at a national level with government health department collaboration. A model for an implementation program that has improved patient outcomes is provided by the national asthma program in Finland, a long-term, comprehensive, multifaceted public health initiative with well-defined targets for asthma guideline implementation.

Public health strategies involving a broad coalition of stakeholders in asthma care, including medical societies, health care professionals, patient support groups, government, and the private sector, have been implemented in Australia (Australian National Asthma Campaign, http://www.nationalasthma.org.au), and

the United States (National Asthma Education and Prevention Program, http://www.nhlbi.nih.gov).

An important part of the implementation process is to establish a system to evaluate the effectiveness and quality of care. Evaluation involves surveillance of traditional epidemiological parameters, such as morbidity and mortality, as well as the specific audit of both process and outcome within different sectors of the health care system. Each country should determine its own minimum sets of data to audit health outcomes. There are a variety of assessment tools which provide a consistent and objective assessment of asthma morbidity or control (e.g., Asthma Control Test, Asthma Control Questionnaire, Asthma Therapy Assessment Questionnaire). Results of these assessments should be recorded at each visit, providing a record of the long-term clinical response of the patient to treatment. Direct feedback provides several benefits—a means for the patient/caregiver to become familiar with, and sensitized to, satisfactory versus poor control of asthma; a reference point from which to evaluate deteriorating asthma; and an indicator of changes in asthma control in response to changes in treatment. The strategy of culturally appropriate direct feedback of clinical outcomes to physicians about specific health care results of their patients may be important for general practitioners who treat many diseases in addition to asthma and thus could not be expected to know guidelines in detail and handle patients accordingly.

See Chapter 5, "Implementation of Asthma Guideline in Health Systems," in the original guideline document for a discussion of the economic value of interventions and guideline implementation in asthma and dissemination and implementation resources.

IMPLEMENTATION TOOLS

Clinical Algorithm
Foreign Language Translations
Patient Resources
Pocket Guide/Reference Cards
Resources
Slide Presentation

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness
Staying Healthy

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Global Initiative for Asthma (GINA), National Heart, Lung and Blood Institute (NHLBI). Global strategy for asthma management and prevention. Bethesda (MD): Global Initiative for Asthma (GINA), National Heart, Lung and Blood Institute (NHLBI); 2008. 92 p. [383 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1995 Jan (revised 2008)

GUIDELINE DEVELOPER(S)

Global Initiative for Asthma - Disease Specific Society

GUIDELINE DEVELOPER COMMENT

The Global Initiative for Asthma (GINA) is a collaborative project of the U.S. National Heart, Lung, and Blood Institute (NHLBI) and the World Health Organization (WHO).

SOURCE(S) OF FUNDING

Not stated

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Global Strategy for Asthma Management and Prevention 2008 Committee

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Disclosures for members of Global Initiative for Asthma (GINA) Executive and Science Committees can be found at: http://www.ginasthma.com/Committees.asp?l1=7&l2=2.

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Global Initiative for Asthma (GINA), National Heart, Lung and Blood Institute (NHLBI). Global strategy for asthma management and prevention. Bethesda (MD): Global Initiative for Asthma (GINA), National Heart, Lung and Blood Institute (NHLBI); 2007. 92 p. [372 references]

In an effort to keep the GINA Workshop report as up to date as possible, a GINA Science Committee has been established to review published research on asthma management and prevention, and to post yearly updates on the GINA Web site. See the GINA Web site for archived versions of the GINA guidelines.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the Global Initiative for Asthma (GINA) Web site.

Print copies: Available from the National Heart, Lung, and Blood Institute (NHLBI), Information Center, P.O. Box 30105, Bethesda, MD 20824-0105 and the Global Initiative for Asthma Secretariat, Professor Jean Bousquet, Service des Maladies Respiratoires, Hopital Arnaud de Villeneuve, 34295, Montpellier, Cedex 5, France

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Pocket guide for asthma management and prevention. Bethesda (MD): Global Initiative for Asthma, National Heart, Lung, and Blood Institute, 2007. Electronic copies: Available from the Global Initiative for Asthma (GINA) Web site.
- Pocket guide for asthma management and prevention in children. Bethesda (MD): Global Initiative for Asthma, National Heart, Lung, and Blood Institute, 2006. Electronic copies: Available from the Global Initiative for Asthma (GINA) Web site.
- GINA teaching slide set. Bethesda (MD): Global Initiative for Asthma, National Heart, Lung, and Blood Institute, 2006. Electronic copies: Available from the Global Initiative for Asthma (GINA) Web site.
- GINA guidelines at-a-glance desk reference. Global Initiative for Asthma, National Heart, Lung, and Blood Institute, 2006. Electronic copies: Available from the Global Initiative for Asthma (GINA) Web site.
- Guideline available in various translations: Electronic copies: Available from the Global Initiative for Asthma (GINA) Web site.
- Other resources. Electronic copies: Available from the Global Initiative for Asthma (GINA) Web site.
- A new table showing current combination therapies will be prepared, posted on the Global Initiative for Asthma (GINA) Web site, and updated as new formulations become available.

Print copies: Available from the National Heart, Lung, and Blood Institute (NHLBI), Information Center, P.O. Box 30105, Bethesda, MD 20824-0105 and the Global Initiative for Asthma Secretariat, Professor Jean Bousquet, Service des Maladies Respiratoires, Hopital Arnaud de Villeneuve, 34295, Montpellier, Cedex 5, France

PATIENT RESOURCES

The following is available:

- You can control your asthma. GINA patient guide. Bethesda (MD): Global Initiative for Asthma, National Heart, Lung, and Blood Institute, 2007 Jun. Electronic copies: Available from the Global Initiative for Asthma (GINA) Web site.

Print copies: Available from the National Heart, Lung, and Blood Institute (NHLBI), Information Center, P.O. Box 30105, Bethesda, MD 20824-0105 and the Global Initiative for Asthma Secretariat, Professor Jean Bousquet, Service des Maladies Respiratoires, Hopital Arnaud de Villeneuve, 34295, Montpellier, Cedex 5, France

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